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Evaluation of ocular surface parameters in children with inflammatory bowel disease

Dry eye in childhood inflammatory bowel disease

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Abstract

Aim: Inflammatory bowel disease (IBD), in the form of ulcerative colitis (UC) or Crohn's disease (CD), is a chronic condition that primarily leads to bowel inflammation but also affects other organ systems via systemic immune response. Involvement of the ocular system can be observed and dry eye is a common problem in IBD patients. There is currently no research that has studied dry eye among children with IBD. In this study, the effects of the chronic inflammatory process on tear production and ocular surface findings were evaluated in pediatric IBD patients.

Material and Methods: Twenty-nine children aged 6-18 years with remission of IBD and 20 healthy children were included in the study. Dry eye disease was studied using the Schirmer test, tear break-up time, corneal staining with the Oxford grading scale, and non-invasive tear break-up time (NTBUT) with videokeratoscopy.

Results: There was a statistically significant difference between UC and CD patients and between CD patients and control subjects in terms of NTBUT (p=0.009 and p=0.033, respectively). A weak positive correlation was found between age and test duration in the patient group (p=0.03, r=0.39).

Discussion: Evaluation of NTBUT with videokeratoscopy can facilitate the early diagnosis of dry eye in pediatric IBD patients. Destructive complications of dry eye and ocular surface inflammation can be prevented with regular follow-up.

Keywords

Ophthalmology, Dry Eye, Inflammatory Bowel Disease

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Introduction

Inflammatory bowel disease (IBD) is a chronic disease triggered by an abnormal elevated inflammatory response of the intestinal mucosa against common enteric bacteria in people who have a genetic predisposition. Ulcerative colitis (UC) and Crohn's disease (CD) are two different forms of IBD [1]. The incidence of IBD is approximately 25-30% up to 20 years, and the disease has a more severe course in pediatric cases than adulthood [2].

IBD in pediatric patients affects growth, development, education, and social life in later years with an increasing incidence. Extraintestinal involvement (EIM) is common in IBD patients, and luminal antigens are thought to be the result of a systemic immune response caused by increased intestinal permeability. Many organs and systems may be affected due to systemic inflammation in IBD patients. Extraintestinal findings may occur in 6-40% of patients with IBD. Extraintestinal symptoms may appear at any time during the disease and may also be the first sign of the disease before intestinal symptoms appear [3]. This process may have a different course than the intestinal inflammatory process. Colitis or ileocolitis is more troublesome for EIMs than isolated small bowel involvement [4]. Joints, eyes, skin, liver, and bile ducts are the most common sites of involvement outside of the gastrointestinal system. Hematological anomalies, increased tendency to thrombosis, and hearing loss are also very common conditions in IBD patients [5-8]. Similar to other extraintestinal findings in IBD, ocular findings may also occur during the course of the disease or before bowel findings are observed. Episcleritis, anterior uveitis, and blepharitis are the most frequent findings of ocular involvement. In addition, the fact that the disease affects the vascular structures is another important reason for the occurrence of ocular system findings in IBD patients. Dry eye is another common eye condition in IBD patients [9, 10]. The tear glands, cornea, and conjunctiva are also affected by this systemic inflammatory process, resulting in impaired tear production [11].

To the best of our knowledge, no studies on dry eye parameters in pediatric IBD patients have been reported. In this research, we focus on how chronic inflammatory processes affect tear production and ocular surface findings in pediatric IBD patients.

Material and Methods

Twenty-nine children aged 6-18 years with IBD in the remission period were included in this study. Twenty healthy children who applied to the ophthalmology clinic for a routine eye examination were enrolled as the control group. Ethics committee approval was obtained from the İstanbul University of Health Sciences Kanuni Sultan Süleyman Training and Research Hospital. The study was conducted in accordance with the Declaration of Helsinki. Before patients were included in the study, detailed information about the study was given and informed consent was obtained. Demographic characteristics of the patients were recorded. Exclusion criteria were preexisting ocular disease such as glaucoma or uveitis, previous ocular surgery, abnormal eyelid position and closure, disorders of the nasolacrimal drainage system, and usage of contact lenses, as well as extraintestinal manifestations of IBD such as episcleritis, corneal infiltrates, and uveitis. Patients and controls were also excluded if they had used any eye drops in the last two weeks before the eye examination. Age, disease duration, and medications used within the 12 months prior to evaluation and concurrent medications were recorded. Two experienced ophthalmologists examined all patients and controls. Each patient underwent full ophthalmologic examination including measurements of best corrected visual acuity using a Snellen chart, slit-lamp examination of the eyelid, and examination of the conjunctiva, cornea, pupils, iris, and fundus. Intraocular pressure was measured by non-contact air puff. Dry eye disease was studied using the Schirmer test, tear break-up time (TBUT), corneal staining with the Oxford grading scale, and non-invasive tear break-up time (NTBUT) with videokeratoscopy (Sirius Scheimpflug-Placido topography system, CSO, Florence, Italy) [12].

For TBUT measurement, a fluorescent-impregnated paper wetted with a drop of sterile saline solution was touched to the lower bulbar conjunctiva and the tear film was examined under cobalt blue light. The time between the last blink and the appearance of the first dry spot was recorded as TBUT, and less than 10 seconds was considered abnormal. Presence of corneal staining with fluorescein is represented by punctate dots on a series of panels. The Oxford grading scale divides corneal staining into six groups according to severity from 0 (absent) to 5 (severe) and the examiner compares the corneal staining pattern [12].

For the Schirmer test, a 35 × 5 mm filter paper strip was used without applying corneal anesthesia. The wetting values of the paper and the amount of tears produced during 5 minutes were calculated by placing the strip on the lateral third of the lower eyelid.

Videokeratoscopy was used for NTBUT measurement. With this method, the integrity of the tear film spread over the anterior surface of the cornea of the patients over time was evaluated. The initial TBUT was expressed as the time (seconds) between the moment the eyelid was opened again after one or more blinks. For videokeratoscopic measurement, the patient's chin was positioned in the appropriate position and with correct focus. When the image became clear, the measurement was started by pressing a joystick button. The system automatically started measuring when the patient blinked twice, and the acquisition automatically stopped after the patient closed his or her eyelid.

Statistical Analysis

SPSS 22 (IBM Corp., Armonk, NY, USA) was used for analyses. The Kolmogorov-Smirnov test was used for assessment of normal distribution. Data were expressed as mean ± standard deviation or median and range for continuous variables; for categorical variables, data were expressed as numbers and percentages (%). Comparisons of groups were made by the Student t-test and Mann-Whitney U tests, while analysis of correlations between variables was performed with the Pearson rank correlation coefficient. Values of $p<0.05$ were considered statistically significant.

Results

This study included 29 IBD patients in remission (8 male,

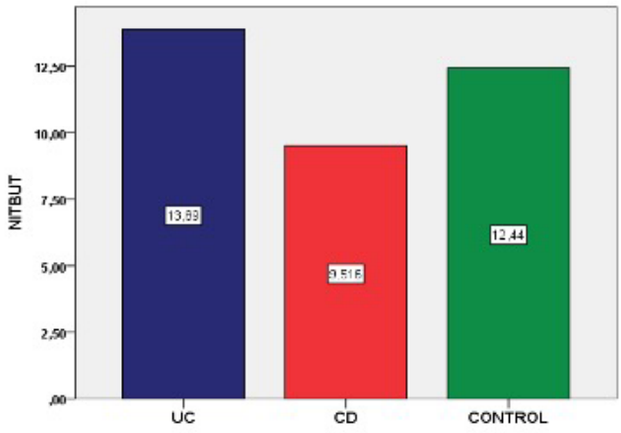

Figure 1. NTBUT results in the UC, CD, and control groups. NTBUT: Non-invasive tear break-up time, UC: ulcerative colitis, CD: Crohn's disease.

21 female; 16 UC, 13 CD; mean age: 14.7±2.64 years) and 20 control subjects (3 male, 17 female). The mean disease duration of the patients was 32.1±12.3 months. Eleven IBD patients were receiving oral mesalamine therapy, 12 patients mesalamine and azathioprine therapy, 4 patients mesalamine and infliximab therapy, 1 patient infliximab-only therapy, and 1 patient mesalamine, infliximab, and azathioprine therapy.

There was no significant difference between the IBD patients and control groups in terms of TBUT (p=0.50), corneal epithelial fluorescein staining (p=0.23), or Schirmer test (p=0.14).

The total test times of videokeratoscopy were 15±2.69 seconds and 15.3±2.7 seconds for the IBD and control groups, respectively, while the NTBUT times were 11.7±5.56 seconds and 12.4±4.9 seconds for the IBD and control groups, respectively. The total test times of videokeratoscopy (p=0.21) and NTBUT (p=0.50) were not significantly different between the IBD and control groups. The NTBUT value of CD patients (9.8±5.8) did not meet the clinical diagnostic criterion for dry eye, but it was found to be significantly lower than the values obtained among the UC patients and the control group (p=0.042).

There was no significant difference between the UC and CD patients in terms of TBUT (p=0.51), corneal epithelial fluorescein staining (p=0.43), Schirmer test (p=0.22), and total test time of videokeratoscopy (p=0.24). NTBUT times were 13.8±4.3 seconds, 9.8±5.8 seconds, and 12.4±4.59 seconds for the UC, CD, and control groups, respectively. There was a statistically significant difference between UC and CD patients and between CD patients and controls in terms of NTBUT (p=0.009 and p=0.033, respectively) (Figure 1).

According to the Pearson rank correlation coefficient, a weak positive correlation was found between age and test duration in the patient group (p=0.03, r=0.39). There was no correlation between drugs used in the treatment of the disease and TBUT, corneal epithelial fluorescein staining, or Schirmer test.

Discussion

IBD is a group of chronic inflammatory diseases that cause systemic, immune-mediated, bowel damage; it is possible that organs and systems beyond the intestines may also be affected by this inflammation [1-3, 13]. The etiopathogenesis of IBD is thought to be the result of a dysregulated immune response to gut microbiota in a genetically predisposed host [1]. EIMs have been confirmed to occur in 25-40% of IBD cases, affecting the musculoskeletal and mucocutaneous systems, the skin, and the hepatobiliary tract. However, EIMs may also occur before the classic signs of the disease are seen [3].

Ophthalmological manifestations of IBD in the literature were first reported by Crohn, who described keratomalacia and xerophthalmia in two UC patients in 1925. The incidence of ocular complications of IBD manifestations are reported to be seen more frequently in cases of CD than UC [14-18].

Knox et al. categorized ocular complications into 3 groups: primary, secondary, and incidental [19]. For the management of primary ocular complications (keratopathy, uveitis, episcleritis, and scleritis), conservative or surgical treatment of the intestinal inflammation is usually sufficient. Secondary ocular complications can occur after primary complications or as a complication of treatment (posterior subcapsular cataract formation as a result of corticosteroid administration, scleromalacia due to scleritis, and night blindness due to hypovitaminosis as a result of a diet low in vegetables or intestinal resection). Conjunctivitis, photophobia, and subconjunctival hemorrhage are ocular symptoms that do not appear to be associated with IBD [20]. Since ocular involvement may precede the emergence of intestinal symptoms, early diagnosis may also be effective in preventing long-term complications of IBD [21]. On the other hand, the presence of ocular symptoms may not necessarily mean the presence of an active intestinal disease flare [22].

In this study, we evaluated dry eye disease in pediatric IBD patients and an age-matched control group. According to our results, there was a significant difference between UC and CD patients and between CD patients and controls in terms of NTBUT as measured by videokeratoscopy. The NTBUT value of CD patients (9.8±5.8) did not meet the clinical diagnostic criterion for dry eye, but it was found to be significantly lower than the values obtained among UC patients and the control group. It was observed that there were no dry eye findings that could be evaluated as clinically significant in the pediatric IBD patients included in this study. There were no differences between the groups in terms of the Schirmer test, TBUT, or corneal epithelial fluorescein staining.

Doğan et al. found that tear film quality was lower in IBD patients compared to a control group, but there was no significant difference in tear film quality between UC and CD patients [20]. Felekis et al. analyzed 60 IBD patients (37 with UC and 23 with CD) in terms of dry eye disease with Schirmer's tests and rose-Bengal corneal staining and concluded that 50% of the patients had dry eye complaints (23). Cury and Moss found that dry eye disease was present in 44% of the patients in their study, with 48 CD patients, 40 UC patients, and 24 controls [24]. Lee et al. examined 36 patients with CD and 25 patients with UC and reported that the most common incidental ocular manifestation was dry eye disease at a rate of 57% compared to 21.3% in the control group [13]. The most common ocular complication in two different countries was reported as dry eye by Cury and Moss [24]. Li et al. reported ophthalmological EIMs including

dry eye disease at a rate of 2% in IBD patients in the Chinese population, a rate significantly lower than those reported in studies of Caucasian patients [25].

Barta et al. compared the tear film parameters and subjective symptoms of dry eye disease in IBD (UC or CD) patients with those of healthy controls and reported that the objective dry eye parameters were better in UC patients than in CD patients. CD patients tended to develop dry eye disease more frequently than UC patients [14]. Curry and Moss stated that aminosalicylic acid (ASA) intake of more than 3 g per day was associated with dry eye [24]. In a cohort study conducted with 305 patients, the frequency of dry eye was found to be 41.7%, and it was reported that symptoms and ocular inflammation were not proportional. Barta et al. did not find any association between ASA treatment and dry eye, but they did find statistical significance in terms of dry eye parameters between the CD and UC groups among patients who received immunosuppressive therapy and TNF-alpha blocking agents [14]. We did not find any statistical significance between CD and UC patients in terms of the drugs used in treatment and dry eye disease.

Conclusion

Regular ophthalmologic follow-up of patients is important not only for dry eye disease but also for early diagnosis and treatment of all possible ophthalmologic complications. The NTBUT is a non-invasive method in comparison to the standard TBUT measurement. Eye examination by NTBUT by videokeratoscopy for pediatric IBD patients may aid in early diagnosis of dry eye. Thus, regular follow-up of these patients may be preventive in terms of complications due to ocular surface inflammation.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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